



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> :  C07D 233/61		A1	(11) International Publication Number: <b>WO 98/31672</b>  (43) International Publication Date: 23 July 1998 (23.07.98)
<p>(21) International Application Number: PCT/US98/00592</p> <p>(22) International Filing Date: 9 January 1998 (09.01.98)</p> <p>(30) Priority Data: 08/785,626 17 January 1997 (17.01.97) US</p> <p>(71) Applicant: PPG INDUSTRIES, INC. [US/US]; One PPG Place, Pittsburgh, PA 15272 (US).</p> <p>(72) Inventors: TANG, Robert, H.; 1017 Summer Ridge Drive, Murrysville, PA 15668 (US). DAMLE, Suresh, B.; Apartment #2307, 4297 Greensburg Pike, Pittsburgh, PA 15221 (US). ESWARAKRISHNAN, Seetha, L.; 1896 Caribou Drive, Allison Park, PA 15101 (US).</p> <p>(74) Agents: STEIN, Irwin, M.; PPG Industries, Inc., One PPG Place, Pittsburgh, PA 15272 (US) et al.</p>		<p>(81) Designated States: CA, CN, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p><b>Published</b>  <i>With international search report.  Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>	

(54) Title: METHOD OF PRODUCING N,N'-DIAZOLE COMPOUNDS

(57) Abstract

Describes a method of producing N,N'-diazole compounds, e.g. N,N'-carbonyldiimidazole, by reacting in an inert solvent, e.g., toluene, a 1-unsubstituted 1H-azole compound, e.g., 1H-imidazole, and a dihalide compound, e.g., phosgene, in the presence of an organic base, e.g., a tertiary amine such as tri(n-butyl)amine. The molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound may range from 1.7:1 to 2.3:1. The organic base: 1-unsubstituted 1H-azole compound molar ratio is 1:1 when the molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound is less than 2:1. The organic base has a basicity greater than that of the 1-unsubstituted 1H-azole compound, and along with its hydrohalide salt is soluble in the inert solvent.

***FOR THE PURPOSES OF INFORMATION ONLY***

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

<b>AL</b>	Albania	<b>ES</b>	Spain	<b>LS</b>	Lesotho	<b>SI</b>	Slovenia
<b>AM</b>	Armenia	<b>FI</b>	Finland	<b>LT</b>	Lithuania	<b>SK</b>	Slovakia
<b>AT</b>	Austria	<b>FR</b>	France	<b>LU</b>	Luxembourg	<b>SN</b>	Senegal
<b>AU</b>	Australia	<b>GA</b>	Gabon	<b>LV</b>	Latvia	<b>SZ</b>	Swaziland
<b>AZ</b>	Azerbaijan	<b>GB</b>	United Kingdom	<b>MC</b>	Monaco	<b>TD</b>	Chad
<b>BA</b>	Bosnia and Herzegovina	<b>GE</b>	Georgia	<b>MD</b>	Republic of Moldova	<b>TG</b>	Togo
<b>BB</b>	Barbados	<b>GH</b>	Ghana	<b>MG</b>	Madagascar	<b>TJ</b>	Tajikistan
<b>BE</b>	Belgium	<b>GN</b>	Guinea	<b>MK</b>	The former Yugoslav	<b>TM</b>	Turkmenistan
<b>BF</b>	Burkina Faso	<b>GR</b>	Greece		Republic of Macedonia	<b>TR</b>	Turkey
<b>BG</b>	Bulgaria	<b>HU</b>	Hungary	<b>ML</b>	Mali	<b>TT</b>	Trinidad and Tobago
<b>BJ</b>	Benin	<b>IE</b>	Ireland	<b>MN</b>	Mongolia	<b>UA</b>	Ukraine
<b>BR</b>	Brazil	<b>IL</b>	Israel	<b>MR</b>	Mauritania	<b>UG</b>	Uganda
<b>BY</b>	Belarus	<b>IS</b>	Iceland	<b>MW</b>	Malawi	<b>US</b>	United States of America
<b>CA</b>	Canada	<b>IT</b>	Italy	<b>MX</b>	Mexico	<b>UZ</b>	Uzbekistan
<b>CF</b>	Central African Republic	<b>JP</b>	Japan	<b>NE</b>	Niger	<b>VN</b>	Viet Nam
<b>CG</b>	Congo	<b>KE</b>	Kenya	<b>NL</b>	Netherlands	<b>YU</b>	Yugoslavia
<b>CH</b>	Switzerland	<b>KG</b>	Kyrgyzstan	<b>NO</b>	Norway	<b>ZW</b>	Zimbabwe
<b>CI</b>	Côte d'Ivoire	<b>KP</b>	Democratic People's	<b>NZ</b>	New Zealand		
<b>CM</b>	Cameroon		Republic of Korea	<b>PL</b>	Poland		
<b>CN</b>	China	<b>KR</b>	Republic of Korea	<b>PT</b>	Portugal		
<b>CU</b>	Cuba	<b>KZ</b>	Kazakhstan	<b>RO</b>	Romania		
<b>CZ</b>	Czech Republic	<b>LC</b>	Saint Lucia	<b>RU</b>	Russian Federation		
<b>DE</b>	Germany	<b>LI</b>	Liechtenstein	<b>SD</b>	Sudan		
<b>DK</b>	Denmark	<b>LK</b>	Sri Lanka	<b>SE</b>	Sweden		
<b>EE</b>	Estonia	<b>LR</b>	Liberia	<b>SG</b>	Singapore		

- 1 -

METHOD OF PRODUCING N,N'-DIAZOLE COMPOUNDS

DESCRIPTION OF THE INVENTION

The present invention relates to a method of producing  
5 N,N'-diazole compounds selected from the group consisting of  
N,N'-carbonyldiazole, N,N-carbonothioicdiazole, and N,N'-  
thionyldiazole compounds. More particularly, the present  
invention relates to a method of preparing such N,N'-diazole  
compounds by reacting a 1-unsubstituted 1H-azole compound with  
10 a dihalide compound, e.g., phosgene, in the presence of an  
inert solvent and an organic base, e.g., a tertiary amine. In  
accordance with an embodiment of the method of the present  
invention, the molar ratio of the 1-unsubstituted 1H-azole to  
the dihalide compound need not exceed 2:1. N,N'-diazole  
15 compounds prepared in accordance with the present invention  
have been found to have acceptable color.

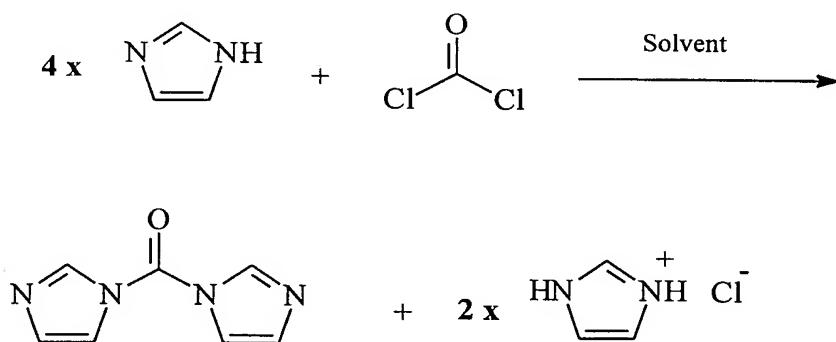
N,N'-diazole compounds, such as N,N'-carbonyldiazole,  
N,N'-carbonothioicdiazole and N,N'-thionyldiazole compounds,  
are useful as reagents for introducing carbonyl,  
20 carbonothioic, thionyl or azole groups into other compounds  
without formation of a hydrohalide acid co-product. They are  
more convenient to handle and easier to measure than dihalide  
compounds, such as phosgene. They are useful in reactions  
involving dehydration, ester formation and isocyanate  
25 formation, and as enzyme and protein binding agents. Further,  
these diazole compounds are also useful as intermediates for  
synthesizing medicines and agricultural chemicals. For  
example, U.S. Patent No. 4,237,709 describes the use of N,N'-  
carbonyldiazole compounds in the preparation of antibiotics  
30 and peptides.

It is known that N,N'-carbonyldiazole, N,N'-  
carbonothioicdiazole and N,N'-thionyldiazole compounds can

- 2 -

each typically be produced by a method involving the reaction of a 1-unsubstituted 1H-azole compound and a dihalide compound such as, respectively phosgene, carbonothioic dichloride and thionyl chloride, each in a molar ratio of 4:1. See for example, W. Forest, Newer Methods of Preparative Organic Chemistry, Volume V, Academic Press, New York (1968) pages 61 - 108. For example, in the case of N,N'-carbonyldiazole compounds, and more specifically N,N'-carbonyldiimidazole, such a prior art method may be represented by the following general scheme I.

General Scheme I



In the above general scheme I, twice as many moles of the 1-unsubstituted 1H-azole compound are used relative to the number of moles of the desired N,N'-carbonyldiazole compound produced. An excess of the 1-unsubstituted 1H-azole compound is required to form a salt with the co-product hydrochloric acid generated in the reaction. Further, in general scheme I the N,N'-carbonyldiazole compound and 1-unsubstituted 1H-azole hydrochloride salt compound precipitate together out of solution at the same time, thus requiring the separation of two intimately mixed solids. Such a separation can be a multi-step process requiring extra time and materials.

The method represented by general scheme I can be expensive in that: (a) only half of the 1-unsubstituted 1H-

- 3 -

azole compound present at the beginning of the reaction is used to form the desired N,N'-carbonyldiazole; and (b) the separation of the precipitated N,N'-carbonyldiazole compound from the precipitated 1-unsubstituted 1H-azole hydrohalide 5 salt is typically a multi-step process requiring additional time and materials. General scheme I is applicative also to the production of N,N'-carbonothioicdiimidazole and N,N'-thionyldimidazole compounds if the appropriate dihalide compound, e.g., carbonothioic dichloride or thionyl chloride, 10 is substituted respectively for phosgene.

United States Patents 3,991,071, 4,080,462 and 4,154,945 disclose a method of preparing carbonylbisimidazole which includes reacting, in an inert solvent, phosgene and 1H-imidazole in the presence of an acid-binding agent. The acid-binding agent is described as being a tertiary amine such as triethylamine, pyridine or excess imidazole. Preferred levels 15 of the acid-binding agent and molar ratios of the acid-binding agent to the 1H-imidazole are not disclosed in United States Patents 3,991,071, 4,080,462 or 4,154,945.

United States Patent 5,552,554 discloses a process of preparing a carbonylating agent, such as N,N'-carbonyldiimidazole or N,N'-carbonyldi(1,2,4-triazole), in-situ by reacting, in the presence of a hydroxyl functional ester and an inert solvent, phosgene and one of 1H-imidazole 20 or 1H-1,2,4-triazole and an organic base selected from the group consisting of trialkylamine, pyridine, picoline or other substituted pyridine. Preferred molar ratios of the organic base to the 1H-imidazole or 1H-1,2,4,-triazole are not disclosed in United States Patent 5,552,554. Examples 2, 5 25 and 11 in columns 7, 8 and 10 respectively of United States Patent 5,552,554 describe in-situ preparations of N,N'-diazoles wherein the molar ratio of the organic base to 1H-

- 4 -

azole compound is in each case greater than 1:1 when the molar ratio of 1-unsubstituted 1H-azole compound to phosgene is less than 2:1.

It has been observed that discolored, e.g., brown, N,N'-diazole compounds can result from the reaction, in an inert solvent, of a 1-unsubstituted 1H-azole compound, e.g., 1H-imidazole, and an excess of a dihalide compound, e.g., phosgene, in the presence of an excess of an organic base such as a tertiary amine. The discoloration has been observed to occur in particular when the molar ratio of the organic base to the 1-unsubstituted 1H-azole compound is greater than 1:1 while at the same time the molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound is less than 2:1.

It would be desirable to have a method of producing N,N'-diazole compounds having a minimum of discoloration, such as N,N'-carbonyldiazole, N,N'-carbonothioicdiazole and N,N'-thionyldiazole compounds, that is more efficient in terms of the utilization of starting materials, and the process of isolating the desired product.

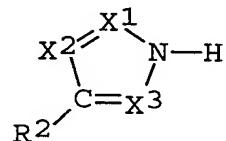
It has now been discovered that N,N'-diazole compounds, such as N,N'-carbonyldiazole compounds, can be produced by reacting a 1-unsubstituted 1H-azole compound and a dihalide compound, e.g., phosgene, in a molar ratio that need not exceed 2:1. It has further been discovered that that N,N'-carbonyldiazole compounds produced in accordance with the present invention have a minimum of discoloration.

In accordance with the present invention, there is provided a method of producing N,N'-diazole compound selected from the group consisting of N,N'-carbonyldiazole, N,N'-carbonothioicdiazole, and N,N'-thionyldiazole compounds, comprising reacting in an inert solvent and in the presence of

- 5 -

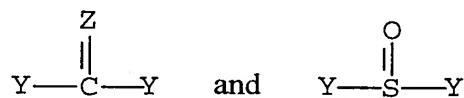
an organic base, a 1-unsubstituted 1H-azole compound represented by the following general formula I:

I



5 wherein  $X^1$ ,  $X^2$  and  $X^3$  are independently  $CR^1$  or nitrogen provided that at least one of  $X^1$ ,  $X^2$  and  $X^3$  is nitrogen,  $R^1$  and  $R^2$  are independently hydrogen, halogen such as chlorine and bromine,  $C_1$  -  $C_6$  alkyl, phenyl, substituted phenyl, or when  $X^3$  is  $CR^1$  together form a fused ring having 4 to 6 carbon atoms

10 inclusive of the two carbon atoms in the 1-unsubstituted 1H-azole ring through which  $R^1$  and  $R^2$  are connected; with a dihalide compound selected from a member of the group consisting of:



15 wherein Z is oxygen or sulfur, and Y is independently fluorine, chlorine or bromine, preferably chlorine.

The molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound can vary from 1.7:1 to 2.3:1, preferably from 1.8:1 to 2:1, and more preferably from 1.9:1 to 2:1. The organic base is soluble in the inert solvent, has a basicity greater than that of the 1-unsubstituted 1H-azole compound, and forms a hydrohalide salt that is soluble in the inert solvent. The molar ratio of the organic base to the 1-unsubstituted 1H-azole compound is 1:1 when the molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound is less than 2:1.

- 6 -

Other than in the operating examples, or where otherwise indicated, all numbers expressing quantities of ingredients or reaction conditions used in the specification and claims are to be understood as modified in all instances by the term  
5 "about".

DETAILED DESCRIPTION OF THE INVENTION

The 1-unsubstituted 1H-azole compounds useful in the method of the present invention contain only one secondary 10 amino group which is located in the 1-position of the azole ring, as described in general formula I above. With reference to R<sup>1</sup> and R<sup>2</sup> of general formula I above, by substituted phenyl is meant C<sub>1</sub> - C<sub>6</sub> alkyl substituted phenyl, halogen, e.g., chlorine and bromine, substituted phenyl or C<sub>1</sub> - C<sub>6</sub> alkyl and 15 halogen substituted phenyl. The substituents R<sup>1</sup> and R<sup>2</sup> are chosen such that they do not preclude the desired reaction at the 1-position.

1-unsubstituted 1H-azole compounds described with reference to general formula I, wherein X<sup>2</sup> is nitrogen, and X<sup>1</sup> 20 and X<sup>3</sup> are each CR<sup>1</sup>, are commonly referred to as 1-unsubstituted 1H-imidazoles, or 1H-imidazoles. Examples of 1H-imidazoles useful in the method of the present invention include, but are not limited to: 1H-imidazole; 1H-4-methylimidazole; 1H-5-methylimidazole; 1H-4-ethyl-5-methylimidazole; 1H-2,4-dimethylimidazole; 1H-2-phenylimidazole; 1H-4-phenylimidazole; 1H-5-phenylimidazole; 25 1H-2,4,5-triphenylimidazole; 1H-2-methyl-4,5-diphenylimidazole; 1H-4-bromoimidazole; 1H-5-bromoimidazole; 1H-4-bromo-5-methylimidazole; 1H-4-methyl-5-bromoimidazole; 1H-4-bromo-5-phenylimidazole; 1H-4-phenyl-5-bromoimidazole; 30 1H-2,4-dibromo-5-methylimidazole; 1H-2,5-dibromo-4-methylimidazole; and 1H-benzimidazole.

- 7 -

1-unsubstituted 1H-azole compounds described with reference to general formula I, wherein  $X^1$  is nitrogen, and  $X^2$  and  $X^3$  are  $CR^1$  are commonly referred to as 1-unsubstituted 1H-pyrazoles or 1H-pyrazoles. Examples of 1H-pyrazoles useful in 5 the method of the present invention include, but are not limited to: 1H-pyrazole; 3,5-dimethyl-1H-pyrazole; and 1H-indazole.

10 1-unsubstituted 1H-azole compounds described with reference to general formula I, wherein  $X^1$  and  $X^2$  are both nitrogen and  $X^3$  is  $CR^1$  are commonly referred to as 1-unsubstituted 1H-1,2,3-triazoles, or 1H-1,2,3-triazoles. Examples of 1H-1,2,3-triazoles useful in the method of the present invention include, but are not limited to, 1H-1,2,3-triazole and 1H-1,2,3-benzotriazole.

15 16 1-unsubstituted 1H-azole compounds described with reference to general formula I, wherein  $X^2$  and  $X^3$  are both nitrogen, and  $X^1$  is  $CR^1$  are commonly referred to as 1-unsubstituted 1H-1,2,4-triazoles, or 1H-1,2,4-triazoles. Examples of 1H-1,2,4-triazoles useful in the method of the 20 present invention include, but are not limited to, 1H-1,2,4-triazole and 1H-5-methyl-1,2,4-triazole.

25 Azole compounds described with reference to general formula I, wherein  $X^1$ ,  $X^2$  and  $X^3$  are each nitrogen are commonly referred to as tetrazoles. Such tetrazoles can be represented by two tautomeric forms, 1H-tetrazole and 2H-tetrazole. Conversion between the two tautomeric forms is thought to occur through a proton shift. While general formula I is representative of tetrazoles having the 2H-tetrazole tautomeric form, it is also meant to be representative of 30 tetrazoles having the more prevalent 1H-tetrazole tautomeric form. Examples of tetrazoles useful in the method of the present invention include, but are not limited to, 1H-

- 8 -

tetrazole, 1H-5-methyl-tetrazole, 1H-5-benzyl-tetrazole and 1H-5-phenyl-tetrazole.

Preferred 1-unsubstituted 1H-azole compounds useful in the method of the present invention include: 1H-imidazole; 1H-5-benzimidazole; 1H-pyrazole; 1H-indazole; 1H-1,2,3-triazole; 1H-1,2,3-benzotriazole; and 1H-1,2,4-triazole. A particularly preferred 1-unsubstituted 1H-azole compound is 1H-imidazole. A single 1-unsubstituted 1H-azole compound or a mixture of such compounds may be used as desired. The use of a single 1-unsubstituted 1H-azole compound is preferred.

In the method of the present invention a 1-unsubstituted 1H-azole compound is reacted with a dihalide compound, as described above, to form N,N'-carbonyldiazole, N,N'-carbonothioicdiazole, or N,N'-thionyldiazole compounds. The 15 molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound may range from 1.7:1 to 2.3:1, preferably from 1.8:1 to 2:1 and more preferably from 1.9:1 to 2:1. Since the desired products of the method of present invention are N,N'-carbonyldiazole, N,N'-carbonothioicdiazole, and N,N'-thionyldiazole compounds, the molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound is preferably 2:1. However, it is understood by those skilled in the art that in large scale practice, i.e., at the commercial production level, an excess of the dihalide compound, e.g., 25 phosgene, may be used. An excess of the dihalide compound, e.g., phosgene, which can be as high as 20% molar excess, is often present because of the difficulty in accurately measuring such dihalide compounds, which are typically in the gas phase under the reaction conditions employed.

30 The method of the present invention is conducted in the presence of an inert solvent as the reaction medium, which is preferably a solvent for the reactants. By inert, it is meant

- 9 -

a solvent which will not interfere or otherwise preclude the reaction between the 1-unsubstituted 1H-azole and dihalide compound. Classes of inert solvents useful in the practice of the present invention include, but are not limited to, 5 alkanes, aromatic solvents, halogenated solvents, ethers, dioxanes, esters, amides and ureas. Halogenated and aromatic solvents are the preferred classes of inert solvents. More specific examples of inert solvents which may be used include: alkanes such as, hexane, heptane and octane; aromatic 10 solvents, such as toluene, benzene, cumene, mesitylene, propylbenzene, anisole and xylene; halogenated solvents, such as methylene chloride, chlorobenzene, and 1,2-dichloroethane; ethers such as, tetrahydrofuran, diethyl ether and 1,2-dimethoxyethane; dioxanes such as 1,4-dioxane; esters such 15 as, methyl acetate and ethyl acetate; amides such as, N,N-dimethylformamide and N-methyl-1,2-pyrrolidine; and ureas such as 1,3-dimethyl-2-imidazolidinone. Preferred inert solvents are the organic solvents methylene chloride and toluene. A particularly preferred inert solvent is toluene. 20 In the method of the present invention, the inert solvent is present in an amount sufficient to solubilize the reactants.

The method of the present invention is conducted also in the presence of an organic base which has a basicity greater than that of the 1-unsubstituted 1H-azole compound. The 25 reaction between the 1-unsubstituted 1H-azole compound and the dihalide compound results in the formation of a hydrohalide acid co-product, e.g., hydrochloric acid in the case of phosgene. By having a basicity greater than that of the 1-unsubstituted 1H-azole compound, is meant that the formation 30 of the hydrohalide salt of the organic base is at least thermodynamically favored, and preferably also kinetically favored, over the formation of the 1-unsubstituted 1H-azole

- 10 -

hydrohalide salt. Hydrohalide salt formation which occurs predominantly between the organic base and the hydrohalide acid, allows the 1-unsubstituted 1H-azole compound to be free to react with the dihalide compound.

5 Any organic base, or mixture of organic bases, which: has a basicity greater than that of the 1-unsubstituted 1H-azole compound; will not form a covalent bond with the dihalide compound; and together with its hydrohalide salt is soluble in the inert solvent of the reaction mixture, may be  
10 used in the practice of the present invention.

In the practice of the present invention, the molar ratio of the organic base to the 1-unsubstituted 1H-azole compound is 1:1, provided the molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound is less than 2:1.

15 When the molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound is less than 2:1, it is necessary that the ratio of the organic base to the 1-unsubstituted 1H-azole compound not exceed 1:1, so that formation of a discolored N,N'-diazole compound is minimized. Without  
20 meaning to be bound by any theory, it is believed that when for example producing N,N'-carbonyldiimidazole in the presence of an excess of phosgene, the excess phosgene reacts with the N,N'-carbonyldiimidazole to form an imidazole carbamoyl chloride which in the presence of excess organic base, e.g., a  
25 tertiary amine such as tri(n-butyl)amine, forms as yet uncharacterized dark colored species.

The presence of the organic base in a molar ratio of 1:1 with the 1-unsubstituted 1H-azole compound, also allows for the use of only that amount of 1-unsubstituted 1H-azole  
30 compound that is desired to be incorporated through covalent bond formation into the N,N'-diazole compound product. For example, in producing N,N'-carbonyldiimidazole by the method

- 11 -

of the present invention, the ratio of 1H-imidazole to the dihalide compound, e.g., phosgene, need not exceed 2:1.

Further, in the practice of the present invention when the molar ratio of the 1-unsubstituted 1H-azole compound to 5 the dihalide compound is equal to 2:1, the molar ratio of the organic base to the 1-unsubstituted 1H-azole compound may be 1:1 or greater. Since the method of the present invention does not require the presence of an excess of the organic base, it is preferable under these circumstances that the 10 molar ratio of the organic base to the 1-unsubstituted 1H-azole compound be 1:1.

Still further, in the practice of the present invention when the molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound is greater than 2:1, the molar ratio 15 of the organic base to the 1-unsubstituted 1H-azole compound may be 1:1 or greater, or the molar ratio of the organic base to the dihalide compound may be 2:1 or greater. Since the method of the present invention does not require the presence of an excess of the organic base, it is preferable under these 20 circumstances that the molar ratio of the organic base to the dihalide compound be 2:1.

In the practice of the present invention, the organic base and its hydrohalide salt are both soluble in the inert solvent of the reaction mixture. This allows for the facile 25 separation of a N,N'-diazole compound that is substantially free of the hydrohalide salt of the organic base. For example, N,N'-carbonyldiimidazole produced according to the method of the present invention may be isolated from the reaction mixture as a precipitate which is substantially free 30 of the hydrohalide salt of the organic base. Although a small amount of the hydrohalide salt of the organic base may be present in the precipitated N,N'-diazole compound, it is

- 12 -

understood by those skilled in the art that the purity of the N,N'-diazole product may be further increased by washing with additional solvent followed by drying.

In the practice of the method of the present invention, 5 the organic base is preferably a tertiary amine. Examples of tertiary amines useful in the method of the present invention include: tri(aryl)amines, e.g., wherein each aryl group contains from 6 to 9 carbon atoms, such as triphenylamine and tribenzylamine; tri(alkyl)amines, such as, trimethylamine, 10 triethylamine, N,N-dimethylethylamine, tri(n-propyl)amine, tri(isopropyl)amine, tri(n-butyl)amine, tripentylamine, trihexylamine, trioctylamine, tridecylamine and tridodecylamine. Other useful tertiary amines include 1-methylpyrrolidine, 1-methylpyrrole and 1-methylpiperidine. 15 The tri(alkyl)amines wherein each alkyl group contains from 1 to 12, e.g., 1 to 6, carbon atoms are preferred, with tri(n-butyl)amine being particularly preferred.

The 1-unsubstituted 1H-diazole and dihalide compounds may be charged to the reactor in any order. They may be 20 introduced concurrently or sequentially. The addition may be continuous or intermittent. In a preferred embodiment of the present invention, an appropriate amount of dihalide compound is slowly introduced into a suitable reaction vessel containing appropriate amounts of inert solvent, 1-unsubstituted 25 1H-diazole compound and tertiary amine.

The temperature at which the reaction of the method of the present invention is conducted may vary considerably, but ordinarily is at a temperature at which the solvent is liquid, and is in the range of from 15°C to 150°C. A temperature of 30 from 50°C to 80°C is preferred, particularly when the inert solvent used is toluene.

- 13 -

The pressure at which the reaction of the method of the present invention is conducted is also subject to wide variation. Atmospheric and slightly superatmospheric pressures are generally employed since the reaction is in the 5 liquid phase, although greater or lesser pressures may be used. Preferably the pressure at which the reaction is conducted is atmospheric pressure.

The present invention is more particularly described in the following examples, which are intended to be illustrative 10 only, since numerous modifications and variations therein will be apparent to those skilled in the art. Unless otherwise specified, all parts and percentages are by weight.

#### EXAMPLE 1

15 This example describes the preparation of N,N'-carbonyldiimidazole by a method approximating that represented in General Scheme I, using the following enumerated ingredients.

20	Ingredients	Amount in grams   moles
<u>Charge 1</u>		
	toluene	605.5   6.6
	1H-imidazole	102.2   1.5
<u>Charge 2</u>		
25	phosgene	40.8   0.41

Charge 1 was added to a 1 liter four-necked flask fitted with a motor-driven stir blade, a temperature probe and heating mantle (both of which were connected to a temperature feed-back control device), a phosgene and nitrogen inlet tube, 30 the outlet of which was set above the liquid surface within the flask, and a cold condenser vented to a caustic scrubber.

- 14 -

The contents of the flask were then heated to a temperature of about 65°C under a nitrogen purge. With the nitrogen purge turned off, Charge 2 was fed into the flask over a period of 20 to 30 minutes, during which time an exotherm peak of 82°C 5 was observed. At the completion of the addition of Charge 2, the contents of the flask were allowed to cool and degas under a nitrogen purge. At the completion of the degassing phase, the contents of the flask were heated to 80°C and filtered under nitrogen through a heated 70 to 100 micron glass fritted 10 filter. The collected solids were washed two times each with 173 grams of toluene heated to a temperature of 80°C. The filtrates were collected into a single vessel and allowed to slowly cool to room temperature with stirring under a nitrogen purge, during which time white crystals began precipitating 15 from the filtrate. The precipitate was collected under nitrogen using a 70 to 100 micron glass fritted filter. The collected precipitate was washed four times each with 99 grams of hexane at room temperature to remove excess toluene. The washed precipitate was then dried with slight heating under a 20 nitrogen sweep. In all, 28 grams of dried precipitate were isolated. The percent yield and summary of process steps are tabulated in Table 1. Analysis of the precipitate is detailed 25 in Table 2.

25

#### EXAMPLE 2

This example describes the preparation of N,N'-carbonyldiimidazole using tri(n-butyl)amine as the organic base, wherein the molar ratio of tri(n-butyl)amine to 1H-imidazole is 1.1:1.0 while the molar ratio of 1H-imidazole to 30 phosgene is less than 2.0:1.0.

- 15 -

Ingredients	Amount in grams   moles	
<u>Charge 1</u>		
5 toluene	250	2.7
tri(n-butyl)amine	103.0	0.56
1H-imidazole	34.0	0.50
<u>Charge 2</u>		
phosgene	25.5	0.26
10 Charge 1 was added to a 1 liter four-necked flask fitted with a motor-driven stir blade, a temperature probe and heating mantle (both of which were connected to a temperature feed-back control device), a phosgene and nitrogen inlet tube, the outlet of which was set above the liquid surface within		
15 the flask, and a cold condenser vented to a caustic scrubber. The contents of the flask were heated to a temperature of about 65°C to 70°C under a nitrogen purge. With the nitrogen purge turned off, Charge 2 was fed into the flask over a period of about 20 minutes, while maintaining the contents of		
20 the flask at a temperature of 70°C to 75°C. At the completion of the addition of Charge 2, the contents of the flask were slowly cooled with constant stirring to and held at room temperature during which time a crystalline precipitate was observed to form. A brown to dark brown colored crystalline		
25 precipitate was separated from the contents of the flask under nitrogen by filtration using a 70 to 100 micron glass fritted filter. The collected brown colored precipitate was next washed three times with 150 grams each of toluene followed by two additional washings with 200 grams each of hexane. The		
30 washed precipitate, which was still brown to dark brown in color, was dried under a nitrogen sweep. In all, 26.5 grams		

- 16 -

of dried brown colored precipitate were isolated. The percent yield and summary of process steps are tabulated in Table 1. Analysis of the precipitate is detailed in Table 2.

5

EXAMPLE 3

*N,N'*-carbonyldiimidazole was prepared in accordance with the method of the present invention using the following enumerated ingredients.

10	Ingredients	Amount in grams   moles
<u>Charge 1</u>		
	toluene	173   1.9
	tri(n-butyl) amine	92.7   0.50
15	1H-imidazole	34.1   0.50
<u>Charge 2</u>		
	phosgene	26.0   0.26

Charge 1 was added to a 500 ml four-necked flask fitted with a motor driven stir blade, a temperature probe and 20 heating mantle (both of which were connected to a temperature feed-back control device), a phosgene and nitrogen inlet tube the outlet of which was set above the liquid surface within the flask, and a cold condenser vented to a caustic scrubber. The contents of the flask were heated to a temperature of 25 about 65°C to 70°C under a nitrogen purge. With the nitrogen purge turned off, Charge 2 was fed into the flask over a period of from 20 to 30 minutes, while maintaining the contents of the flask at a temperature of 70°C to 75°C. At 30 the completion of the addition of Charge 2, the contents of the flask were cooled with constant stirring to 20°C to 25°C over a period of 1 to 1.5 hours, and then held at that

- 17 -

temperature for an additional 30 to 45 minutes. A white crystalline precipitate was separated from the contents of the flask under nitrogen by filtration using a 70 to 100 micron glass fritted filter. The collected precipitate was next 5 washed with 346 grams of toluene and then dried with slight heating under a nitrogen sweep. In all, 32.5 grams of dried precipitate was isolated. The percent yield and summary of process steps are tabulated in Table 1. Analysis of the precipitate is detailed in Table 2.

10

TABLE 1

		<u>Results</u>		
		Example 1	Example 2	Example 3
15	Test			
	% Yield <sup>a</sup>	42%	65%	76%
	Number of filtrations. <sup>b</sup>	2	1	1
20	Grams of 1H-imidazole used per gram of precipitate collected. <sup>c</sup>	3.7	1.3	1.1

<sup>a</sup> The % Yield was determined using the following equation, 25  $100 \times (\text{actual grams of precipitate collected} / \text{theoretical grams of product})$ .

<sup>b</sup> The number of filtrations required from the completion of the reaction within the flask to the isolation of the final 30 precipitated product.

<sup>c</sup> The amount of 1H-imidazole added to the reaction at the beginning of the reaction over the grams of precipitate 35 collected.

The data of Table 1 shows that the method of the present invention is more efficient than that of the prior art method represented in General Scheme I, in terms of producing N,N'-

- 18 -

carbonyldiimidazole. When compared to the prior art method, as represented by Example 1, the method of the present invention, as represented by Example 3, produces a higher yield of product while using less raw materials, i.e. 1H-5 imidazole.

**TABLE 2**  
Analysis of the Isolated Precipitated Product  
of Examples 1, 2 and 3.

10		Results		
		Example 1	Example 2	Example 3
15	Test			
	Visual appearance	White	Brown	White
20	% Weight N,N'-Carbonyldiimidazole <sup>d</sup> (by CO <sub>2</sub> evolution analysis)	98.7%	N.D. <sup>1</sup>	100.7%
25	% Weight N,N'-Carbonyldiimidazole <sup>e</sup> (by G.C. analysis)	N.D.	N.D.	99.5%
	% Weight Tri(n-butyl)amine <sup>e</sup> (by G.C. analysis)	N.A. <sup>2</sup>	N.D.	0.08%
30	% Weight Toluene <sup>e</sup> (by G.C. analysis)	N.D.	N.D.	0.06%
	% Weight Ionic Chloride <sup>f</sup> (by AgNO <sub>3</sub> titration)	0.44%	N.D.	0.07%

<sup>1</sup>N.D. = Not Determined.

35 <sup>2</sup>N.A. = Not Applicable.

<sup>d</sup> This analysis is based on the reaction: one mole of N,N'-carbonyldiimidazole + one mole of H<sub>2</sub>O, in the presence of a protic acid, will produce two moles of 1H-imidazole and one mole of CO<sub>2</sub>.

- 19 -

<sup>e</sup> G.C. (Gas Chromatograph). The percent weight of N,N'-carbonyldiimidazole, tri(n-butyl)amine and toluene present in the isolated precipitated product of Examples 1 and 2 were determined here using standard gas chromatographic methods. A 5 Hewlett Packard 5890E gas chromatograph fitted with a column having the following specifications, HP-5 30 M x 0.32 mm i.d. with 0.25 micron film, was used.

<sup>f</sup> The % Weight Ionic Chloride was determined by dissolving a 10 known amount of the isolated precipitated product in water acidified with nitric acid, followed by potentiometric titration of the chloride ion (anion) with AgNO<sub>3</sub> using a silver billet electrode to detect the end point. This method is not specific as to the source of the chloride ion.

15

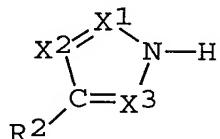
The data of Table 2 shows that the method of the present invention, as represented by Example 3, results in the production of N,N'-carbonyldiimidazole having a white color 20 which is essentially equivalent to that of the prior art method represented by Example 1. The data of Table 2 also shows the criticality of maintaining the molar ratio of the tertiary amine to 1H-imidazole at 1:1 when the molar ratio of 1H-imidazole to phosgene is less than 2:1, in comparing 25 Examples 2 and 3.

The present invention has been described with reference to specific details of particular embodiments thereof. It is not intended that such details be regarded as limitations upon the scope of the invention except insofar as and to the extent 30 that they are included in the accompanying claims.

- 20 -

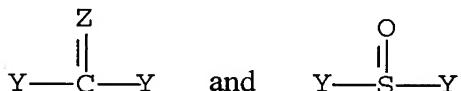
We claim:

1. A method of producing N,N'-diazole compound selected from the group consisting of N,N'-carbonyldiazole, N,N'-carbonothioicdiazole and N,N'-thionyldiazole compounds, comprising reacting in an inert solvent:
  - (a) 1-unsubstituted 1H-azole compound represented by the following general formula,



wherein  $\text{X}^1$ ,  $\text{X}^2$  and  $\text{X}^3$  are independently  $\text{CR}^1$  or nitrogen provided that at least one of  $\text{X}^1$ ,  $\text{X}^2$  and  $\text{X}^3$  is nitrogen;  $\text{R}^1$  and  $\text{R}^2$  are independently hydrogen, halogen,  $\text{C}_1 - \text{C}_6$  alkyl, phenyl, substituted phenyl, or when  $\text{X}^3$  is  $\text{CR}^1$  together form a fused ring having 4 to 6 carbon atoms inclusive of the two carbon atoms in the 1-unsubstituted 1H-azole ring through which  $\text{R}^1$  and  $\text{R}^2$  are connected; and

- (b) a dihalide compound selected from a member of the group consisting of



wherein Z is oxygen or sulfur, and Y is independently fluorine, chlorine or bromine, the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound being from 1.7:1 to 2.3:1, in the presence of an organic base that is soluble in said inert solvent and that has a basicity greater than that of said 1-unsubstituted 1H-azole compound, the molar ratio of said organic base to said 1-unsubstituted 1H-azole compound being 1:1 when the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound is

- 21 -

less than 2:1, thereby producing said N,N'-diazole compound and a hydrohalide salt of said organic base, said hydrohalide salt being soluble in said inert solvent.

5 2. The method of claim 1 wherein when  $X^3$  is  $CR^1$  and  $R^1$  and  $R^2$  together form a fused ring, said fused ring is a benzene ring.

10 3. The method of claim 1 wherein  $X^1$  and  $X^3$  are  $CR^1$  and  $X^2$  is nitrogen.

4. The method of claim 3 wherein  $R^1$  and  $R^2$  are each hydrogen.

15 5. The method of claim 1 wherein Y is chlorine or bromine.

6. The method of claim 5 wherein Y is chlorine.

20 7. The method of claim 6 wherein said dihalide compound is phosgene.

25 8. The method of claim 1 wherein the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound is from 1.8:1 to 2:1.

9. The method of claim 8 wherein the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound is from 1.9:1 to 2:1.

30

10. The method of claim 1 wherein said organic base is a tertiary amine.

- 22 -

11. The method of claim 10 wherein said organic base is selected from at least one of the group consisting of N,N-dimethylethyl amine, tri(n-propyl)amine, tri(isopropyl)amine and tri(n-butyl)amine.

12. The method of claim 11 wherein said organic base is tri(n-butyl)amine.

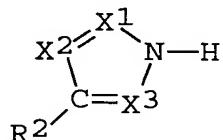
10 13. The method of claim 1 wherein said inert solvent is selected from the group consisting of aromatic solvents and halogenated solvents.

14. The method of claim 13 wherein said inert solvent is 15 an aromatic solvent.

15. The method of claim 14 wherein said inert solvent is toluene.

20 16. A method of producing N,N'-carbonyldiazole compounds, comprising reacting in an inert solvent:

(a) 1-unsubstituted 1H-azole compound represented by the following general formula,

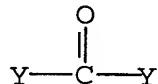


25 wherein X<sup>1</sup>, X<sup>2</sup> and X<sup>3</sup> are independently CR<sup>1</sup> or nitrogen provided that at least one of X<sup>1</sup>, X<sup>2</sup> and X<sup>3</sup> is nitrogen; R<sup>1</sup> and R<sup>2</sup> are independently hydrogen, halogen, C<sub>1</sub> - C<sub>6</sub> alkyl, phenyl, substituted phenyl, or when X<sup>3</sup> is CR<sup>1</sup> together form a fused ring having 4 to 6 carbon atoms inclusive of the two carbon

- 23 -

atoms in the 1-unsubstituted 1H-azole ring through which R<sup>1</sup> and R<sup>2</sup> are connected; and

(b) a dihalide compound represented by the following general formula,



5

wherein Y is independently fluorine, chlorine or bromine, the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound being from 1.7:1 to 2.3:1, in the presence of an organic base that is soluble in said inert solvent and 10 that has a basicity greater than that of said 1-unsubstituted 1H-azole compound, the molar ratio of said organic base to said 1-unsubstituted 1H-azole compound being 1:1 when the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound is less than 2:1, thereby producing said 15 N,N'-carbonyldiazole compound and a hydrohalide salt of said organic base, said hydrohalide salt being soluble in said inert solvent.

17. The method of claim 16 wherein when X<sup>3</sup> is CR<sup>1</sup> and R<sup>1</sup> 20 and R<sup>2</sup> together form a fused ring, said fused ring is a benzene ring.

18. The method of claim 16 wherein X<sup>1</sup> and X<sup>3</sup> are CR<sup>1</sup>, X<sup>2</sup> 25 is nitrogen, Y is chlorine, said inert solvent is selected from the group consisting of aromatic solvents and halogenated solvents, and said organic base is a tertiary amine.

19. The method of claim 18 wherein R<sup>1</sup> and R<sup>2</sup> are each hydrogen, said organic base is tri(n-butyl)amine, said inert 30 solvent is an aromatic solvent, and the molar ratio of said 1-

- 24 -

unsubstituted 1H-azole compound to said dihalide compound is from 1.8:1 to 2:1.

20. The method of claim 19 wherein said inert solvent is 5 toluene, and the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound is from 1.9:1 to 2:1.

# INTERNATIONAL SEARCH REPORT

Intern. Appl. Application No  
PCT/US 98/00592

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 6 C07D233/61

According to International Patent Classification(IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WALTER W ET AL: "Zur Umsetzung von Azolen mit anorganischen Säurechloriden" LIEBIGS ANNALEN DER CHEMIE., no. 11, 1979, WEINHEIM DE, pages 1756-1767, XP002064142 see the whole document; in particular page 1757, 1st paragraph, and page 1761, 7th paragraph</p> <p>---</p> <p>BEYERMAN H C ET AL: "Use of Carbonylditriazole in Peptide Synthesis" RECUEIL DES TRAVAUX CHIMIQUES DES PAYS-BAS., vol. 80, no. 11, November 1961, AMSTERDAM NL, pages 1372-1375, XP002064143 see page 1373, footnote 6</p> <p>---</p> <p style="text-align: right;">-/--</p>	1,16
X		1,16

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

<sup>a</sup> Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

4

Date of the actual completion of the international search

8 May 1998

Date of mailing of the international search report

26/05/1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Fink, D

**INTERNATIONAL SEARCH REPORT**Intern. Application No  
PCT/US 98/00592

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 552 554 A (STERNBERG JEFFREY A ET AL) 3 September 1996 cited in the application see the whole document; in particular the examples 2, 5, 10 and 11 -----	1-20
A	US 3 991 071 A (BROOKES ROBERT F ET AL) 9 November 1976 cited in the application see column 25 - column 26; example 7 see column 7, line 54 - line 66 -----	1-20

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern:  Application No  
PCT/US 98/00592

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 5552554 A	03-09-96	AT 149157 T		15-03-97
		AU 674042 B		05-12-96
		AU 5544094 A		08-06-94
		DE 69308317 D		03-04-97
		DE 69308317 T		04-09-97
		EP 0668859 A		30-08-95
		ES 2098901 T		01-05-97
		HU 71639 A		29-01-96
		JP 8502994 T		02-04-96
		WO 9411359 A		26-05-94
		PL 308908 A		04-09-95
<hr/>				
US 3991071 A	09-11-76	GB 1469772 A		06-04-77
		ZA 7408037 A		28-01-76
		US 4080462 A		21-03-78
		BE 860966 A		18-05-78
		CS 188185 B		28-02-79
		CY 995 A		02-08-79
		DD 113164 A		20-05-75
		DE 2429523 A		16-01-75
		FR 2234293 A		17-01-75
		JP 1286805 C		31-10-85
		JP 50031047 A		27-03-75
		JP 60010003 B		14-03-85
		KE 2940 A		30-03-79
		US 4154945 A		15-05-79
<hr/>				



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> :  C07D 233/61		A1	(11) International Publication Number:  <b>WO 98/31672</b>
			(43) International Publication Date: 23 July 1998 (23.07.98)
(21) International Application Number: PCT/US98/00592	(22) International Filing Date: 9 January 1998 (09.01.98)		(81) Designated States: CA, CN, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).
(30) Priority Data: 08/785,626 17 January 1997 (17.01.97) US			<b>Published</b> <i>With international search report.</i> <i>With amended claims and statement.</i>
(71) Applicant: PPG INDUSTRIES, INC. [US/US]; One PPG Place, Pittsburgh, PA 15272 (US).			<b>Date of publication of the amended claims and statement:</b> 3 September 1998 (03.09.98)
(72) Inventors: TANG, Robert, H.; 1017 Summer Ridge Drive, Murrysville, PA 15668 (US). DAMLE, Suresh, B.; Apartment #2307, 4297 Greensburg Pike, Pittsburgh, PA 15221 (US). ESWARAKRISHNAN, Seetha, L.; 1896 Caribou Drive, Allison Park, PA 15101 (US).			
(74) Agents: STEIN, Irwin, M.; PPG Industries, Inc., One PPG Place, Pittsburgh, PA 15272 (US) et al.			

## (54) Title: METHOD OF PRODUCING N,N'-DIAZOLE COMPOUNDS

## (57) Abstract

Describes a method of producing N,N'-diazole compounds, e.g. N,N'-carbonyldiimidazole, by reacting in an inert solvent, e.g., toluene, a 1-unsubstituted 1H-azole compound, e.g., 1H-imidazole, and a dihalide compound, e.g., phosgene, in the presence of an organic base, e.g., a tertiary amine such as tri(n-butyl)amine. The molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound may range from 1.7:1 to 2.3:1. The organic base: 1-unsubstituted 1H-azole compound molar ratio is 1:1 when the molar ratio of the 1-unsubstituted 1H-azole compound to the dihalide compound is less than 2:1. The organic base has a basicity greater than that of the 1-unsubstituted 1H-azole compound, and along with its hydrohalide salt is soluble in the inert solvent.

***FOR THE PURPOSES OF INFORMATION ONLY***

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

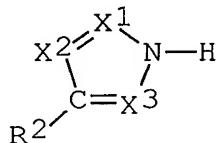
<b>AL</b>	Albania	<b>ES</b>	Spain	<b>LS</b>	Lesotho	<b>SI</b>	Slovenia
<b>AM</b>	Armenia	<b>FI</b>	Finland	<b>LT</b>	Lithuania	<b>SK</b>	Slovakia
<b>AT</b>	Austria	<b>FR</b>	France	<b>LU</b>	Luxembourg	<b>SN</b>	Senegal
<b>AU</b>	Australia	<b>GA</b>	Gabon	<b>LV</b>	Latvia	<b>SZ</b>	Swaziland
<b>AZ</b>	Azerbaijan	<b>GB</b>	United Kingdom	<b>MC</b>	Monaco	<b>TD</b>	Chad
<b>BA</b>	Bosnia and Herzegovina	<b>GE</b>	Georgia	<b>MD</b>	Republic of Moldova	<b>TG</b>	Togo
<b>BB</b>	Barbados	<b>GH</b>	Ghana	<b>MG</b>	Madagascar	<b>TJ</b>	Tajikistan
<b>BE</b>	Belgium	<b>GN</b>	Guinea	<b>MK</b>	The former Yugoslav Republic of Macedonia	<b>TM</b>	Turkmenistan
<b>BF</b>	Burkina Faso	<b>GR</b>	Greece	<b>ML</b>	Mali	<b>TR</b>	Turkey
<b>BG</b>	Bulgaria	<b>HU</b>	Hungary	<b>MN</b>	Mongolia	<b>TT</b>	Trinidad and Tobago
<b>BJ</b>	Benin	<b>IE</b>	Ireland	<b>MR</b>	Mauritania	<b>UA</b>	Ukraine
<b>BR</b>	Brazil	<b>IL</b>	Israel	<b>MW</b>	Malawi	<b>UG</b>	Uganda
<b>BY</b>	Belarus	<b>IS</b>	Iceland	<b>MX</b>	Mexico	<b>US</b>	United States of America
<b>CA</b>	Canada	<b>IT</b>	Italy	<b>NE</b>	Niger	<b>UZ</b>	Uzbekistan
<b>CF</b>	Central African Republic	<b>JP</b>	Japan	<b>NL</b>	Netherlands	<b>VN</b>	Viet Nam
<b>CG</b>	Congo	<b>KE</b>	Kenya	<b>NO</b>	Norway	<b>YU</b>	Yugoslavia
<b>CH</b>	Switzerland	<b>KG</b>	Kyrgyzstan	<b>NZ</b>	New Zealand	<b>ZW</b>	Zimbabwe
<b>CI</b>	Côte d'Ivoire	<b>KP</b>	Democratic People's Republic of Korea	<b>PL</b>	Poland		
<b>CM</b>	Cameroon	<b>KR</b>	Republic of Korea	<b>PT</b>	Portugal		
<b>CN</b>	China	<b>KZ</b>	Kazakhstan	<b>RO</b>	Romania		
<b>CU</b>	Cuba	<b>LC</b>	Saint Lucia	<b>RU</b>	Russian Federation		
<b>CZ</b>	Czech Republic	<b>LI</b>	Liechtenstein	<b>SD</b>	Sudan		
<b>DE</b>	Germany	<b>LK</b>	Sri Lanka	<b>SE</b>	Sweden		
<b>DK</b>	Denmark	<b>LR</b>	Liberia	<b>SG</b>	Singapore		

## AMENDED CLAIMS

[received by the International Bureau on 22 July 1998 (22.07.98);  
original claims 1, 11, 16, 18 and 19 amended; original claim 10 cancelled,  
remaining claims unchanged (5 pages)]

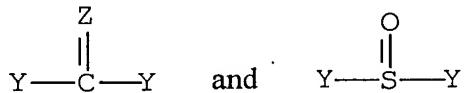
1. A method of producing N,N'-diazole compound selected from the group consisting of N,N'-carbonyldiazole, N,N'-carbonothioicdiazole and N,N'-thionyldiazole compounds, 5 comprising reacting in an inert solvent:

(a) 1-unsubstituted 1H-azole compound represented by the following general formula,



wherein X<sup>1</sup>, X<sup>2</sup> and X<sup>3</sup> are independently CR<sup>1</sup> or nitrogen, 10 provided that at least one of X<sup>1</sup>, X<sup>2</sup> and X<sup>3</sup> is nitrogen; R<sup>1</sup> and R<sup>2</sup> are independently hydrogen, halogen, C<sub>1</sub> - C<sub>6</sub> alkyl, phenyl, substituted phenyl, or when X<sup>3</sup> is CR<sup>1</sup>, R<sup>1</sup> and R<sup>2</sup> together form a fused ring having 4 to 6 carbon atoms inclusive of the two carbon atoms in the 1-unsubstituted 1H-azole ring through 15 which R<sup>1</sup> and R<sup>2</sup> are connected; and

(b) a dihalide compound selected from a member of the group consisting of



wherein Z is oxygen or sulfur, and Y is independently 20 fluorine, chlorine or bromine, the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound being from 1.7:1 to 2.3:1, in the presence of a tertiary amine selected from the group consisting of tri(alkyl)amines, wherein each alkyl group contains from 3 to 12 carbon atoms, 25 and tribenzylamine, said tertiary amine being soluble in said inert solvent and having a basicity greater than that of said 1-unsubstituted 1H-azole compound, the molar ratio of said

- 26 -

tertiary amine to said 1-unsubstituted 1H-azole compound being 1:1 when the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound is less than 2:1, thereby producing said N,N'-diazole compound and a hydrohalide salt of 5 said tertiary amine, said hydrohalide salt being soluble in said inert solvent.

2. The method of claim 1 wherein when  $X^3$  is  $CR^1$  and  $R^1$  and  $R^2$  together form a fused ring, said fused ring is a benzene 10 ring.

3. The method of claim 1 wherein  $X^1$  and  $X^3$  are  $CR^1$  and  $X^2$  is nitrogen.

15 4. The method of claim 3 wherein  $R^1$  and  $R^2$  are each hydrogen.

5. The method of claim 1 wherein Y is chlorine or 20 bromine.

6. The method of claim 5 wherein Y is chlorine.

7. The method of claim 6 wherein said dihalide compound is phosgene.

25 8. The method of claim 1 wherein the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound is from 1.8:1 to 2:1.

30 9. The method of claim 8 wherein the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound is from 1.9:1 to 2:1.

- 27 -

11. The method of claim 1 wherein said tertiary amine is selected from at least one of the group consisting of N,N-dimethylethyl amine, tri(n-propyl)amine, tri(isopropyl)amine 5 and tri(n-butyl)amine.

12. The method of claim 11 wherein said organic base is tri(n-butyl)amine.

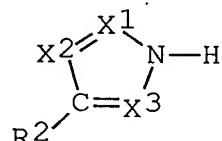
10 13. The method of claim 1 wherein said inert solvent is selected from the group consisting of aromatic solvents and halogenated solvents.

14. The method of claim 13 wherein said inert solvent 15 is an aromatic solvent.

15. The method of claim 14 wherein said inert solvent is toluene.

20 16. A method of producing N,N'-carbonyldiazole compounds, comprising reacting in an inert solvent:

(a) 1-unsubstituted 1H-azole compound represented by the following general formula,

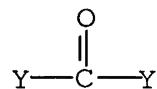


25 wherein X<sup>1</sup>, X<sup>2</sup> and X<sup>3</sup> are independently CR<sup>1</sup> or nitrogen provided that at least one of X<sup>1</sup>, X<sup>2</sup> and X<sup>3</sup> is nitrogen; R<sup>1</sup> and R<sup>2</sup> are independently hydrogen, halogen, C<sub>1</sub> - C<sub>6</sub> alkyl, phenyl, substituted phenyl, or when X<sup>3</sup> is CR<sup>1</sup>, R<sup>1</sup> and R<sup>2</sup> together form a fused ring having 4 to 6 carbon atoms inclusive of the two

- 28 -

carbon atoms in the 1-unsubstituted 1H-azole ring through which R<sup>1</sup> and R<sup>2</sup> are connected; and

(b) a dihalide compound represented by the following general formula,



5

wherein Y is independently fluorine, chlorine or bromine, the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound being from 1.7:1 to 2.3:1, in the presence of a tertiary amine selected from the group consisting of 10 tri(alkyl)amines, wherein each alkyl group contains from 3 to 12 carbon atoms, and tribenzylamine, said tertiary amine being soluble in said inert solvent and having a basicity greater than that of said 1-unsubstituted 1H-azole compound, the molar ratio of said tertiary amine to said 1-unsubstituted 1H-azole 15 compound being 1:1 when the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound is less than 2:1, thereby producing said N,N'-carbonyldiazole compound and a hydrohalide salt of said tertiary amine, said hydrohalide salt being soluble in said inert solvent.

20

17. The method of claim 16 wherein when X<sup>3</sup> is CR<sup>1</sup> and R<sup>1</sup> and R<sup>2</sup> together form a fused ring, said fused ring is a benzene ring.

25

18. The method of claim 16 wherein X<sup>1</sup> and X<sup>3</sup> are CR<sup>1</sup>, X<sup>2</sup> is nitrogen, Y is chlorine and said inert solvent is selected from the group consisting of aromatic solvents and halogenated solvents.

- 29 -

19. The method of claim 18 wherein R<sup>1</sup> and R<sup>2</sup> are each hydrogen, said tertiary amine is tri(n-butyl)amine, said inert solvent is an aromatic solvent, and the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound is 5 from 1.8:1 to 2:1.

20. The method of claim 19 wherein said inert solvent is toluene, and the molar ratio of said 1-unsubstituted 1H-azole compound to said dihalide compound is from 1.9:1 to 2:1.

10

- 30 -

### STATEMENT UNDER ARTICLE 19

Enclosed herewith are replacements for pages 20-24 of the subject application in which amendments to the claims are made. The difference between the claims as filed and the claims as amended are as follows:

- a) Claims 1, 11, 16, 18 and 19 have been amended;
- b) Claim 10 has been cancelled; and
- c) Claim 2-9, 12-15, 17 and 20 remain unchanged.

Claims 1 and 16 have been amended to include omitted language when R<sup>1</sup> and R<sup>2</sup> together form a fused ring, which disclosure can be found on page 5, lines 6-11, and to amend the definition OF the organic base to be a tertiary amine selected from the group consisting of tri(alkyl)amines wherein each alkyl group contains from 3 to 12 carbon atoms and tribenzylamine. Basis for the later amendment may be found on page 12, lines 4-13 of the specification. Amendments to claims 11, 18 and 19 change the reference to the organic base to that of a tertiary amine in accordance with the amendments to claims 1 and 16.

The amendments to the claims which amend the definition of the organic base to certain tertiary amines has been made for the reason that the lower tertiary amines such as triethyl amine are not appropriate for the claimed invention because they result in the formation of a precipitated hydrohalide salt - the claims requiring the hydrohalide salt to be soluble in the inert solvent. An amendment to the description to place the disclosure in accord with the amended claims will be made under Article 34 when appropriate.